Reviewer's report

**Title:** Exploring the Uncertainties of Early Detection Results: Model-Based Interpretation of Mayo Lung Project

**Version:** 2  **Date:** 4 November 2010

**Reviewer:** Deborah L Goldwasser

**Reviewer's report:**

In general, the writing of this paper represents a significant improvement over the prior submission. There are features of the analysis that concern me with respect to the methodology.

The model which predicts the true underlying burden of disease is based on a calibration to SEER data. The simulated total incidence appears to under-predict the number of cancers detected in the MLP screening arm. Therefore, screening sensitivity parameters are estimated to be close to 1. I don’t think these estimates are realistic, and it may be that the MLP population had a higher risk of lung cancer than the SEER population to which the Weibull distribution was calibrated. Under these conditions, it is no surprise that increasing the risk of lung cancer in the screening arm improves the deviance measure, because the incidence model under-predicted cancers in the screening arm under perfect sensitivity.

The simple model, assuming perfect sensitivity, predicts 188 cancers in the intervention arm whereas the control arm predicts 184, a difference of four cancers. The true difference between the two arms was 46. So, it seems that in essence the model fit is improved by re-assigning lung cancers from the control arm into the screening arm, assuming that most cancers that are present are detected in the course of the study. I don’t find this result particularly believable. With a slightly higher total incidence model, a wider range of results are equally likely.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.